NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Cipaglucosidase alfa with miglustat for treating Pompe disease

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of cipaglucosidase alfa with miglustat within its marketing authorisation for treating Pompe disease.

Background

Pompe disease, also known as glycogen storage disease type II or acid maltase deficiency is a rare inherited genetic disorder caused by the mutation of the GAA gene which makes an enzyme called acid alpha-glucosidase, resulting in the deficiency of this enzyme.[1] This leads to the progressive accumulation of glycogen, a sugar usually stored in multiple tissues including around the heart, skeletal muscles, respiratory muscles, vascular, gastrointestinal and nervous systems.[1,2] The signs and symptoms of Pompe disease are directly related to the muscles affected. The respiratory, skeletal and cardiac muscles are most profoundly affected. Other symptoms include pain, mental fatigue and an impact on mental health.

Pompe disease is classified in two subtypes. The infantile onset and the late onset. The late onset can present from 1 year of age and is characterised by a progressive myopathy (with little or no cardiac involvement) which can lead to severe morbidity, respiratory failure and early mortality.[3,4] While acid alpha-glucosidase activity is typically absent or nearly absent in infantile onset Pompe disease, there is still some residual activity present in those with late onset Pompe disease.[5]

In 2019 in the EU, Pompe disease was estimated to affect approximately 0.3 in 10,000 people.[6] In 2018 in the EU, the reported birth prevalence was 0.8 per 100,000 people for the infantile onset form and 1.75 per 100,000 for the late-onset form according to European Orphanet data.[7]

Current clinical management includes enzyme replacement therapy (ERT) with alglucosidase alfa which aims to replace the missing or malfunctioning enzyme. The decision to start treatment is usually based on a set of criteria including confirmed diagnosis and the patient should be symptomatic, have residual skeletal and respiratory muscle function and not have another advanced stage life-threatening condition.[8] Supportive treatment is also needed and can include physiotherapist, occupational therapist, speech therapist and dietetician.[3]

The technology

Cipaglucosidase alfa (brand name unknown, Amicus Therapeutics Europe Ltd) is a second-generation, glycoengineered recombinant acid alpha glucosidase replacement therapy. It is used in combination with miglustat. Cipaglucosidase alfa has a higher amount of Mannose 6 phosphate (M6P) compared with alglucosidase alfa leading to an improved binding to cation-independent Mannose 6 phosphate receptors (CI-MPR) and cellular uptake. Cipaglucosidase alfa is administered intravenously.

Miglustat is a pharmacological chaperone that protects cipaglucosidase alfa from denaturation in systemic circulation and improves the delivery of active cipaglucosidase alfa to lysosomes. Miglustat is administered orally.

Neither cipaglucosidase alfa nor miglustat currently have marketing authorisations in the UK for treating Pompe disease. Cipaglucosidase alfa with miglustat has been studied in clinical trials compared with alglucosidase alfa in adults with late-onset Pompe disease. It has been studied in adults who have received enzyme replacement therapy with alglucosidase alfa and also in adults who have not. It has also been studied in children with late onset Pompe disease who have received enzyme replacement therapy with alglucosidase alfa and also in children who have not.

Intervention(s)	Cipaglucosidase alfa with miglustat
Population(s)	People with Pompe disease
Comparators	Alglucosidase alfa
Outcomes	The outcome measures to be considered include: • change in respiratory function • change in motor function • change in muscular function • mortality • immunogenicity response • adverse effects of treatment • health-related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or

	outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
Other considerations	If the evidence allows the following subgroups will be considered: • people who have received prior treatment with alglucosidase alfa • people who have not received prior treatment with alglucosidase alfa The availability and cost of biosimilar and generic products should be taken into account. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Avalglucosidase alfa for treating Pompe disease [ID3737]. Publication date to be confirmed.
Related National Policy	NHS England (2018) Highly specialised services 2018 (Lysosomal storage disorders service (children & adults) NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' Manual for prescribed specialised services 2018/19, 71. Lysosomal storage disorder service (adults and children) NHS standard contract for metabolic disorders (children, 2013/2014) NHS standard contract for metabolic disorders (laboratory services, 2013/2014) Department of Health & Social Care (2019) The UK strategy for rare diseases: 2019 update to the

	Implementation Plan for England

Questions for consultation

Have all relevant comparators for cipaglucosidase alfa with miglustat been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for treating Pompe disease?

- Do treatment options differ if people have been previously treated with enzyme replacement therapy with alglucosidase alfa?

Are the outcomes listed appropriate?

- Are the subgroups listed under "other considerations" appropriate?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which cipaglucosidase alfa with miglustat will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider cipaglucosidase alfa with miglustat to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of cipaglucosidase alfa with miglustat can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

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4. Van der Ploeg AT, Reuser AJ. Pompe's disease. Lancet. 2008 Oct 11;372(9646):1342-53. Available from: https://www.ncbi.nlm.nih.gov/pubmed/18929906

5. Chan J, Desai AK, Kazi ZB, Corey K, Austin S, Hobson-Webb LD, et al. The emerging phenotype of late-onset Pompe disease: A systematic literature review. Molecular genetics and metabolism. 2017 Mar 1;120(3):163-72. Available from: https://www.sciencedirect.com/science/article/pii/S1096719216302967

6. European Medicines Agency (EMA). Miglustat for the treatment of glycogen storage disease type II (Pompe's disease). Available from: https://www.ema.europa.eu/en/documents/orphan-designation/eu/3/18/2129-public-summary-opinion-orphan-designation-miglustat-treatment-glycogen-storage-disease-type-ii_en.pdf

7. Orphanet – Prevalence and incidence of rare diseases: Bibliographic data. Available from

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